

CLAIMS

1. A pharmaceutical composition for treating or preventing arthritis or other degenerative disease in an individual, said composition comprising a polypeptide comprising a collagen type IX alpha 1 chain NC4 domain or biologically active fragment having anti-arthritic or anti-inflammatory activity in combination with a pharmaceutically acceptable carrier.
2. A pharmaceutical composition for inducing tolerance in an individual to at least one antigenic component of cartilage, said composition comprising a polypeptide comprising a collagen type IX alpha 1 chain NC4 domain or biologically active fragment having anti-arthritic or anti-inflammatory activity in combination with a pharmaceutically acceptable carrier.
3. The composition according to claim 1 or claim 2 wherein the polypeptide has a molecular weight of less than 30,000Da.
4. The composition according to any one of claims 1 to 3 wherein the polypeptide has an amino acid length of less than 250 amino acids.
5. The composition according to any one of claims 1 to 4 wherein the collagen type IX alpha 1 chain NC4 domain comprises
 - (i) an amino acid sequence as provided in SEQ ID NO 1, SEQ ID NO 14, SEQ ID NO 16, or SEQ ID NO 18,
 - (ii) an amino acid sequence which is at least 70% identical to either SEQ ID NO 1, SEQ ID NO 14, SEQ ID NO 16, or SEQ ID NO 18, or
 - (iii) a biologically active fragment of (i) or (ii).
6. The composition according to any one of claims 1 to 4 wherein the collagen type IX alpha 1 chain NC4 domain comprises an amino acid sequence which is at least 90% identical to any one of SEQ ID NO 1, SEQ ID NO 14, SEQ ID NO 16, or SEQ ID NO 18.
7. The composition according to any one of claims 1 to 4 wherein the collagen type IX alpha 1 chain NC4 domain comprises:
 - (i) an amino acid sequence as provided in residues 21-182 of SEQ ID NO 1; residues 60-181 of SEQ ID NO 1; residues 72-181 of SEQ ID NO 1, residues 98-182 of SEQ ID NO 1, or residues 123-182 of SEQ ID NO 1; or
 - (ii) an amino acid sequence as provided in residues 24 - 268 of SEQ ID NO 14; residues 29 - 268 of SEQ ID NO 14, residues 29 - 215 of SEQ ID NO 14, residues 29-209 of SEQ ID NO 14, residues 29 - 208 of SEQ ID NO 14, residues 29 - 96 of SEQ ID NO 14, or residues 108 - 208 of SEQ ID NO 14.

8. The composition according to any one of claims 1 to 4 wherein the collagen type IX alpha 1 chain NC4 domain comprises at least one of SEQ ID NOS 2-11.
9. A method of inducing tolerance in an individual to at least one antigenic component of cartilage comprising administering the individual with an effective amount of the pharmaceutical composition according to any one of claims 1-8.
10. A method for preventing a musculoskeletal degenerative condition in an individual comprising administering a pharmaceutically effective amount of a composition according to any one of claims 1 to 8.
11. A method for preventing an autoimmune response to at least one antigenic component of cartilage comprising administering a composition according to any one of claims 1 to 8.
12. Use of a polypeptide comprising a collagen type IX alpha 1 chain NC4 domain or biologically active fragment having anti-arthritis or anti-inflammatory activity in combination with a pharmaceutically acceptable carrier in the manufacture of a medicament for inducing tolerance to at least one antigenic component of cartilage.
13. Use according to claim 12 wherein the polypeptide has a molecular weight of less than 30,000Da.
14. Use according to claim 12 or 13, wherein the polypeptide has an amino acid length of less than 250 amino acids.
15. Use according to claim 12 wherein the individual is a naive individual.
16. Use of a polypeptide comprising a collagen type IX alpha 1 chain NC4 domain or biologically active fragment having anti-arthritis or anti-inflammatory activity in combination with a pharmaceutically acceptable carrier in the manufacture of a medicament for preventing a musculoskeletal degenerative condition in an individual.
17. Use according to claim 16 wherein the polypeptide has a molecular weight of less than 30,000Da.
18. Use according to claim 16 or 17, wherein the polypeptide has an amino acid length of less than 250 amino acids.
19. A method for recovering a polypeptide having anti-arthritis or anti-inflammatory activity comprising isolating a mixture comprising a GAG-peptide and a polypeptide having a molecular weight of less than 30,000Da by autolysis from connective tissue, separating the GAG-peptide from the polypeptide, and recovering the polypeptide.
20. A method for preparing a polypeptide having anti-arthritis or anti-inflammatory activity, the method comprising

- (i) incubating a connective tissue in an autolysis medium that provides a buffered pH range of between about pH 2.5 and about pH 8.5 for a time and under conditions sufficient to release a GAG-peptide and a polypeptide having a molecular weight of less than 30,000Da,
- 5 (ii) recovering a mixture comprising the GAG-peptide and polypeptide from the autolysis medium;
- (iii) separating the polypeptide from the GAG-peptide; and
- (iv) recovering the polypeptide having a molecular weight of less than 30,000Da.

21. A connective tissue derived polypeptide having anti-arthritis or anti-inflammatory activity, which is obtainable by:

- (i) incubating a connective tissue in an autolysis medium that provides a buffered pH range of between about pH 2.5 and about pH 8.5 for a time and under conditions sufficient to release a GAG-peptide and a polypeptide having a molecular weight of less than 30,000Da,
- 15 (ii) recovering a mixture comprising the GAG-peptide and polypeptide from the autolysis medium;
- (iii) separating the polypeptide from the GAG-peptide; and
- (iv) recovering the polypeptide having a molecular weight of less than 30,000Da.

22. A connective tissue derived polypeptide of claim 21 comprising a collagen type IX alpha 1 chain NC4 domain or biologically active fragment.

23. A pharmaceutical composition comprising one or more connective tissue derived polypeptides having anti-arthritis or anti-inflammatory, wherein said polypeptide is obtainable by a method comprising isolating a mixture comprising a GAG-peptide and a polypeptide having a molecular weight of less than 30,000Da by autolysis from connective tissue, separating the GAG-peptide from the polypeptide, and recovering the polypeptide.

24. A method for preventing a musculoskeletal degenerative condition in an individual comprising administering the individual with an effective amount of a pharmaceutical composition according to claim 23.

30 25. A method for preventing an autoimmune response in an individual to at least one antigenic component of cartilage comprising administering the individual with an effective amount of a pharmaceutical composition according to claim 23.

26. A method of inducing cartilage formation in an individual, comprising administering to the individual an effective amount of a connective tissue derived polypeptide according to claim 23.

27. Use of one or more connective tissue derived polypeptides having anti-arthritis or anti-inflammatory, in the preparation of a medicament for the treatment or prevention of arthritis or other musculoskeletal disease in a subject, wherein said polypeptide is obtainable by the method comprising isolating a mixture comprising a GAG-peptide and a polypeptide having a molecular weight of less than 30,000Da by autolysis from connective tissue, separating the GAG-peptide from the polypeptide, and recovering the polypeptide.
28. Use of one or more connective tissue derived polypeptides having anti-arthritis or anti-inflammatory, in the preparation of a medicament for tolerising an individual to at least one antigenic component of cartilage, wherein said polypeptide is obtainable by a method comprising isolating a mixture comprising a GAG-peptide and a polypeptide having a molecular weight of less than 30,000Da by autolysis from connective tissue, separating the GAG-peptide from the polypeptide, and recovering the polypeptide having a molecular weight of less than 30,000Da.